

Aorta: Few small atheromata.

Bone-marrow: Marked postmortem change.

Microscopic Diagnoses: Primary carcinoma of the lung with extension into the superior vena cava and metastasis to the liver. Thrombosis of the superior vena cava. Bronchopneumonia. Pulmonary edema. Organizing pleuritis. Congestion and hyaline changes in the spleen. Congestion and edema of the liver, kidneys and adrenals. Arteriosclerosis.

NOTE.—This is not a "joint article," but a clinical paper, plus a pathological report. The pathologist never saw the clinical paper; he is not responsible for the opinions expressed therein, and since he never saw the patient during life, any clinical opinions must of necessity have been mine, except where noted as being O'Hara's. I have therefore retained the expression of "my" opinions.

H. W. D.

AN ENDOCRINAL FACTOR IN GENERAL PARESIS.

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It has for many years puzzled psychiatrists why it is that of the great number of persons who are infected with syphilis only a few, probably less than 3 per cent of the total number, eventually develop general paresis. In seeking an answer to this question it is necessary to proceed along two natural lines. The first one is to show, if possible, that the difference rests in the spirochete—that there are strains of spirochete and that the ultimate development of general paresis is a patient depends upon infection with a certain syphilitic strain. The second is to seek out inherent peculiarities of the individual which would cause that individual to develop the paresis.

It is now generally acknowledged that general paresis follows in habitual quasi-constant fashion the syphilis of the benign initial type, and recognized that the likelihood of the development of general paresis in a case of syphilis is in inverse proportion to the occurrence of peripheral ectodermic reaction in the earlier course. The individual who after luetic infection does not show strong ectodermic lesions is more liable eventually to develop paresis. This clinical observation alone does not help to settle the question whether a special neurotropic strain of spirochete determines the paresis or whether the inherent constitutional condition of the individual determines it. The data which I have been able to bring together bear out the second phase of the question and show that the endocrinial

status of the individual has at least a discernible influence in the situation.

Experimental work has been done by various workers to demonstrate that a neurotropic form of spirochete is distinct from a so-called dermatropic virus.

Wile and De Kruif experimented with material obtained from a living paretic brain, and this material was injected into rabbits. They found that subcultures from the rabbits grew much more slowly and much less luxuriously than those cultivated from early cutaneous or mucous-membrane syphilitides.

In 1916 Reasoner was able to demonstrate fixed differences in various strains of syphilis as studied in the rabbit. Choroiditis and choro-retinitis were observed in rabbits inoculated with two different strains of syphilis, and in one strain whose characteristics were not known. In a series of fourteen other strains obtained from chancre and mucus lesions such lesions were not observed.

Milian, writing in 1920, regards it is established that there are different kinds of spirochete, so that the term parasyphilis for tabes and general paresis in his estimation is correct. He believes that the difference between general syphilis and tabes and general paresis is analogous to the difference between typhoid and paratyphoid.

In the past year Marie and Levaditi have reported extensive researches in this field. What they refer to as neurotropic virus they obtained from either the blood, brain substance or spinal fluid of a case of paresis, and their dermatropic virus was in the beginning obtained from a chancre. They report differences as regards inoculation time in rabbits, type of lesion produced, ability of transference from rabbit to monkey and from rabbit to man, and in immunology. They conclude that the spirochete of general paresis must be considered as a different variety from the spirochete causing cutaneous and visceral syphilis.

Though others have believed that in experimental syphilis differences in virulence as well as differences in the period of incubation, and in the character of the lesion can arise through difference in technic, the weight of evidence is in favor of the existence of strains of spirochete.

Yet even granting that there are strains or types of virus differing in evasiveness or predilection for certain tissues the individual resistance of the infected person must still be studied as influencing the form which a syphilitic infection may take.

The almost total absence of general paresis among Arab syphilitics has long attracted attention. Poret and Sengis point out that not even the stress of years of service at the front brought any increase in general paresis among the Arab troops. At Algiers, notwithstanding the extreme prevalence of syphilis, they encountered but one instance of general paresis, and that was of such mild form that the Arab officer was able to serve for more than three years at the

front after the onset of the disease. In China and Japan osseous syphilis is frequent, but nervous syphilis is rare. It would take one into speculative fields to attempt an exact correlation between racial and endocrinial factors, as we at present know them, and that attempt will not be made here.

In the New York State Hospital statistics, though the admissions to the State Hospital show the sexes to be almost evenly represented—for the year ending June 30, 1917, there were 1047 male admissions and 1037 female—there is a marked difference in the number of admissions for paresis—almost three times as many men as women (72 men and 28 women). Since we have no statistics to prove that syphilis occurs more frequently in men than in women, the far higher occurrence of paresis among men stands without explanation. One is led to wonder if the endocrinial condition of men is more favorable toward syphilis taking the paretic form than the endocrinial status of women.

Thus peculiarities concerning the occurrence of paresis as regards race and sex can be cited, and it is probably true that endocrinial factors lie at the base of each.

Long since struck by the infrequency of associated status lymphaticus and paresis I examined a group of 82 unselected cases of general paresis in the Manhattan State Hospital for the purpose of finding what percentage of them gave the signs of status lymphaticus and, further, to classify them into grades according as their external appearance and makeup removed them from the status lymphaticus type.

Status lymphaticus can be safely made a matter of inspection alone, for it can be recognized by the slenderness of the long bones, by the absence of facial and sterno-pectoral hair and by the presence of a feminine type of demarcation of pubic hair. Also the axillary and pubo-anal trichosis is reduced in amount. In the status lymphaticus individual there is a feminine-like rounding or molding out of the contour of the arms and legs. This feature becomes less conspicuous in the individuals of middle life. Though additional signs of status lymphaticus are found only on the autopsy table, it is the opinion of pathologists that the margin of difference in ratios obtained clinically and at autopsy is negligible. I examined the cases of paresis by inspection alone and made my classification on the points above mentioned.

Of the 82 individuals I found only 2 outspoken cases of status lymphaticus. Fifteen, Group 2, showed a low degree of trichosis, not accompanied by the skeletal proportion or other features of the true status lymphaticus condition. Twenty-six cases, Group 3, were average in trichosis. In the fourth group, made up of 21 cases, there was great and more than average trichosis, with the hairy development limited to the body areas normally showing hair in the males. In yet a fifth group, made up of 18 cases, are found the individuals in whom the hairy coat is very excessive, in whom the

distribution leaves almost no part of the body free. Thus, out of 82 cases of paresis only 17 fell below the average in trichosis while 39 ranged above the average. First, it is clear that there was a low occurrence of *status lymphaticus* among the 82 cases of paresis. Among 5652 autopsies in Bellevue Hospital, Symmes has reported 457 cases of *status lymphaticus*. This rate pertains to both sexes considered together. The rate for men considered alone is higher—10 per cent. The occurrence of only 2.43 per cent among male paretics is in sharp contrast. The great percentage of the hypertrichotic types among the paresis cases is striking.*

In Group 3, the average trichosis group, the duration of symptoms from onset to the death of the patient (14 cases dead) averaged 36.7 months and for Group 2, hypotrichotic, but not *status lymphaticus* (7 cases dead), the duration of symptoms averaged thirty-six months. Neither of the 2 *status* individuals has died. Regarding the hypertrichosis groups the average for Group 4 (12 cases dead) was 33.5 months and for Group 5 (8 cases dead) twenty-eight months. Thus the average duration is appreciably reduced for the groups showing hypertrichosis and most reduced for the group showing the hypertrichosis in greatest degree. Also, in the hypertrichotic groups (4 and 5) 50 per cent of the cases died in less than two years from the onset of the disease, while of Groups 2 and 3 (average and hypotrichosis) only 29.5 per cent died in less than two years. In addition, of these latter two groups 43 per cent lived more than three years after the onset while of Groups 4 and 5 (hypertrichotic) only 30 per cent lived more than three years. These percentages in conjunction with the figures previously put down appear to indicate that general paresis besides showing a greater incidence in individuals with hypertrichosis on the average runs a more rapid course in such individuals.

Regarding the first of these apparent relationships, some will want to suggest that *status lymphaticus* cases and near-*status* cases are inherently less liable to lead a life conducive to infection with syphilis, and that this would be an all-important factor in preventing that type of individual from appearing later in the same proportion among paretic cases. No such explanation, however, explains the data bearing on the second phase—namely, that the course of the paresis is hastened. It was impossible to tabulate the antiluetic treatment which these cases had had during their period of hectic infection. They were not under treatment once they had progressed to the point of commitment into the State Hospital. They were, as before stated, unselected cases, and it was thought possible to consider the previous antiluetic treatment as a common factor in them, probably, if known, surprisingly of an average all told.

* In addition it has been possible to correlate the groups with the duration of the disease in a portion of the series. A majority of the clinical examinations were made over a year ago, and recently it was possible to record the length of the disease in a series which had died.

Symmers mentions the almost constant occurrence of hypoplasia of the suprarenal cortex in subjects of *status lymphaticus*. Apert has elaborated his observations regarding the clinical manifestations of suprarenal hyperplasia according to the age of the individual, and believes that for all ages hypertrichosis is a symptom of suprarenal hyperplasia. These references, with numerous others which could be added, show that observations to date connect hypertrichosis with hyperplastic suprarenal functioning. Trichosis in an individual becomes a measure of suprarenal valence and excessive hypertrichosis probably marks the type with the strongest suprarenal chemistry. This, applied to the figures which I have previously given, suggests that heightened suprarenal functioning in the individual is one factor to influence the syphilitic infection in him to assume the special general paretic type and to hasten the course once it is started.

Briefly the conclusions are: (1) The endocrinial status of the individual has a discernible influence in determining whether, once infected with syphilis, he is likely to develop paresis; (2) *status lymphaticus* is rare among male cases of paresis and is seen less frequently among paretics than among autopsied hospital male cases; (3) individuals who have low suprarenal functioning appear to develop paresis less frequently than strong suprarenal individuals; (4) the course of general paresis on the average varies in rapidity directly with the suprarenal strength of the individual.

Discussion. These observations lead me to believe that an estimation of the suprarenal status of an individual at the outset of general paresis can become not alone an index of the probable course of the disease, but also an index of the individual's probable response to treatment—that the weak suprarenal type can be held in check by medication in a manner quite impossible with his opposite in type. Once we accept this observation one's approach in the treatment of paretic cases would be to change by some means the chemistry of the individual in order to pervert any existent suprarenal predominance. This effort would be an adjunct to the usual antiluetic treatment and in no sense a substitute for it. Although methods to alter suprarenal predominance are not known with scientific accuracy at the present time, certain lines of endocrinial therapy suggest themselves and may prove successful. This phase of the question needs long clinical observation, and must be held for later reporting.*

* Symmers states that *status lymphaticus* was found six times more frequently in men than in women. In one series of 249 cases of *status lymphaticus*, 212 were men and 37 women. On the same proportion, of the 457 cases discovered in the larger series 392 were men and 65 women. The sex of the 5670 cases autopsied is not recorded in Symmers's article or ascertainable with an absolute exactitude. However, as in Bellevue Hospital 67 per cent of the autopsies are on males, it is fair to estimate that 3787 were men and 1865 women. Two hundred protocols of autopsies in 1908, 100 in 1910 and 200 in 1914 were reviewed in order to arrive at the average percentage 67 per cent. Therefore, out of 3787 autopsies of men, 392 cases of *status lymphaticus* were found, an occurrence of 10.35 per cent.

The courtesy of Dr. Marcus B. Heyman, superintendent of the Manhattan State Hospital, in permitting me to examine and report concerning cases in that hospital is gratefully acknowledged.

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CHRONIC LYMPHATIC LEUKEMIA ASSOCIATED WITH EXTENSIVE AMYLOIDITIS, ADVANCED NEPHRITIS AND ORAL SEPSIS.

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THE following case is of particular interest, because it exemplifies one of the more unusual conditions which occasionally are associated with leukemia—namely, amyloid infiltration of the viscera in conjunction with an advanced nephritis. The patient was admitted to the medical service of Dr. Leroy H. Briggs at the San Francisco City and County Hospital, and I am indebted to Dr. Briggs for the following clinical history.

Case History. The patient was a married woman, aged forty-eight years, of American birth, who entered the hospital in April, 1920, complaining of chronic bronchitis. The family history and the past history were unimportant. The present illness dated from 1917, when she was treated at the Lane Hospital for leukemia. The following data, covering a period from November, 1917 to July, 1918, were obtained from the records of the Lane Hospital. The first recorded blood examination was made in the out-patient department on November 6, 1917:

Hemoglobin, 55 per cent. Red blood cells, 2,230,000. White blood cells, 10,000.

Differential count: Polymorphonuclear neutrophils, 34 per cent.; large mononuclears, 5 per cent; small mononuclears, 5 per cent; polymorphonuclear eosinophils, 1 per cent; polymorphonuclear basophils, 1 per cent; myelocytes, 3 per cent. One normoblast was present.